

REMARKS

By this Amendment, the specification and claims 1 and 11 are amended. Claims 26-49 and 52 have been withdrawn from consideration pursuant to a restriction requirement. Claims 1-52 are pending.

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

The courtesy of Examiners S. Chunduru and J. Fredman in granting an interview to Applicants on January 15, 2002 is gratefully acknowledged. The interview was granted with the understanding from Group Director Gary Jones that Examiner Wilder is on maternity leave and that this application will be reassigned to Examiner Chunduru based on the filing of this paper by the January 18, 2002 deadline for response. Applicants' separate record of the substance of the interview is incorporated into the following remarks.

Attached hereto is a paper, captioned "Amendment Appendix" showing the marked-up version of the changes made by this Amendment. It will be seen from the Appendix that no new matter is added by this Amendment.

Election/Restriction

The Office Action asserts that there would be a serious burden on the Office to examine all of the pending claims in this

application because: (1) "the searches of the different Groups are not coextensive in the art since methods of hybridization and binding assays as claimed in Groups II and III are not necessarily combined or required for multiplex structures" and (2) the multiplex structure of Group I can be used in other materially different process[es] besides hybridization methods of binding assays." Neither of these rationales justifies restricting claims to a composition (claims 1-25 and 50) from claims to a method for making that composition (claims 26-49). While the art(s) to be searched may not be completely coextensive, the overlap in this matter is likely to be significant. In addition, while the multiplex structure of claim 1 might be used in other methods, the method of base claim 26 can only be used to produce the multiplex structure of claim 1, by definition. Accordingly, Applicants request further reconsideration and withdrawal of the restriction requirement.

Objection

In response to the requirement for a drawing, Applicants attach proposed Fig. 6, and amend the specification to make reference to the new figure. Examiners Fredman and Chunduru approved of the new figure when it was shown to them at the interview. The figure will be submitted to the Drafting Branch of the PTO upon approval by the Examiner. Accordingly,

reconsideration and withdrawal of the objection are respectfully requested.

Rejections under Sections 102 and 103

As agreed at the interview, the applied references do not disclose or suggest multiplexes containing Watson-Crick triplets. See the corresponding Interview Summary, which states: "Discussed novel triplex and quadruplex DNA structures comprising Watson-Crick triplets" (emphasis added). The "wherein" clause added to claim 1 by this Amendment requires the presence of at least one Watson-Crick triplet in the claimed multiplex.

The rejection of claims 1, 3, 4, 6, 20-22 and 51 as being anticipated by Sen et al. '897 is respectfully traversed.

The Office Action asserts that Sen et al. '897 teaches four stranded complexes in claim 1, but the preamble of '897 claim 1 states: "A double stranded nucleic acid complex"

Sen et al. '897 does teach G-quartets, but such four-stranded structures are not associated on the basis of W-C bonding, as required by amended claim 1. See, e.g., Figs. 6a, 6b and 7 of Sen et al. '897, which show that the association of four strands is through contiguous guanine domains, wherein binding is exclusively G-G among all four strands, and contrary to W-C specific binding. See also Sen et al. at column 4, lines 4-7, which states "The 'mismatched' base-pairs in the guanine domain have the property of

additionally binding or 'synapsing' to 'mismatched' base-pairs in another guanine domain to form stable guanine quartets."

As the '897 patent fails to identically disclose each and every limitation of the claimed invention, the '897 patent does not anticipate the claimed invention. Accordingly, reconsideration and withdrawal of the anticipation rejection of claims 1, 3, 4, 6, 20-22 and 51 are respectfully requested.

The rejection of claims 7, 8 and 10 as being obvious over Sen et al. '897 is respectfully traversed.

The '897 patent fails to identically disclose or suggest each and every limitation of base claim 1 for the reasons discussed above. As the '897 patent does not disclose or suggest W-C bonded quadruplexes for the reasons noted above, there is no basis to assume that the groove association limitations of claims 7, 8 and 10 are in the '897 patent.

Furthermore, the '897 patent teaches away from the claimed invention at, e.g., column 7, lines 1-24, which concludes: "The high negative charge-density along the backbone of the double-helix, as well as the absence of possibilities for further base-pairing, create a net repulsive interaction between any two double helices." That is, the '897 patent teaches that G-quartets overcome the inability of quadruplexes to form on the basis of

Watson-Crick specific recognition and binding by previously W-C paired duplex nucleic acids.

Accordingly, reconsideration and withdrawal of the obviousness rejection of claims 7, 8 and 10 are respectfully requested.

The rejection of claims 1, 4-6, 11-19 and 23-25 as allegedly being obvious over Hogan et al. '503 is respectfully traversed.

The '503 patent does not disclose quadruplexes as claimed in amended claim 1. Hogan et al. teaches branched nucleic acid structures consisting of exclusively duplex arms wherein one base of each strand binds to no more than one base of another strand (see, e.g., Figs. 6G, 6H and 21). There is no disclosure or suggestion of a specific interaction of any base with more than one base at the same time.

Regarding claim 5, there is no disclosure that each strand comprises an uncharged or partially charged backbone (defined at page 6, first paragraph of application as being less negatively charged than native DNA).

Amended claim 11 further distinguishes over the '503 patent, in requiring that each nucleobase in the second sequence and the fourth sequence binds to two other nucleobases.

Regarding claim 25, the teaching of the '503 patent that the fourth strand contains about 58% purine bases and about 39% pyrimidine bases is nothing unusual for a system in which only

conventional Watson-Crick duplexes are formed in each arm. The significance of the recitation in claim 25 becomes apparent when true quadruplexes are being formed.

Accordingly, reconsideration and withdrawal of the rejection over Hogan and the other rejections under Sections 102 and 103 are respectfully requested.

Utility/Enablement

Although the issues of utility and enablement were not raised in the Office Action, Examiner Fredman suggested that Applicants clarify how the application enables a useful and credible invention. Examiner Fredman explained that he tends to look more closely at the level of enablement/credible utility with pioneering inventions exhibiting a high level of novelty, such as the present one.

More specifically, Examiner Fredman explained that he would want to see evidence that the claimed multiplex is not merely an example of strand invasion that has been misinterpreted by the inventors. Accordingly, Applicants enclose a Rule 132 Declaration of Dr. Jasmine Daksis, which shows that the multiplexes of the invention are not strand-invaded duplexes because: (1) strand invasion is a phenomenon driven by nucleobase-containing sequences having uncharged or partially charged backbones (such as PNA), whereas the overwhelming bulk of Applicants' results relating to

mixed sequence triplex formation and all of the quadruplex binding results are obtained from nucleic acids having normally (i.e., completely) charged backbones; and (2) Applicants' data show that increasing salt concentration does not hinder the formation of the multiplexes, whereas strand invasion decreases with increasing salt concentration due to increased stability of duplexes present.

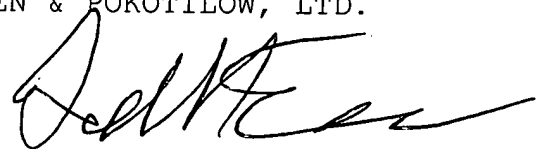
For at least the reasons set forth above, it is respectfully submitted that the above-identified application is in condition for allowance. Favorable reconsideration and prompt allowance of the claims are respectfully requested.

Should the Examiner believe that anything further is desirable in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,

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